UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Jasmin Jackson, Risk Manager

From: Virna Stillwaugh, PhD, Entomologist

Secondary Review: Jennifer Saunders, PhD, Senior Entomologist

Date: 10/8/2020

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD (DER)

THIS DER DOES NOT CONTAIN CONFIDENTIAL BUSINESS INFORMATION

Note: MRIDs found to be **unacceptable** to support label claims should be removed from the data matrix.

DP barcode: 458797
Decision no.: 563470
Submission no: 1052796
Action code: R340
Product Name: Thermacell Radius Zone Mosquito Repellent VI
EPA Reg. No or File Symbol: 71910-11
Formulation Type: Spatial Repellent
Ingredients statement from the label with PC codes included:
Metofluthrin 5.5%, PC code: 109709

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 or mg/kg body weight as appropriate): 1 device will create a 20ft protection zone. Place devices 20 ft apart from each other.

Use Patterns: Battery-powered metofluthrin emitting device product. For outdoor use only.

I. Action Requested: The registrant has submitted 1 MRID (51176601) with new field product performance data for their products Thermacell Radius Zone Repellent VI and Thermacell MR300 Portable Mosquito Repeller Area Repellents against biting mosquito populations using a non-human test method, for review.

II. Background: Thermacell Repellents, Inc. is submitting new data for the already registered product (EPA Reg. No. 71910-11) under an R340 amendment, to revise the product area coverage.

III. MRID Summary:
MRID 51176601. Carroll, S. (2019) Field Evaluation of Thermacell Radius Zone Repellent VI and Thermacell MR300 Portable Mosquito Repeller Area Repellents Against Biting Mosquito Populations Using a Non-Human Test Method. Project Number: TCL/008. Unpublished Study Prepared by Carroll-Loye Biological Research. 257p.

(1) **GLP**

(2) **Methods**:
The objective of this study was to determine the efficacy of Thermacell® Radius Zone Repellent VI (5.5% metofluthrin) against mosquitoes using a Non-Human test method, within a defined area. The registrant submitted comparative data for another product, Thermacell® MR300 Mosquito Repeller (21.97% d-cis/trans-alletrin) consisting of an MR300 emitter with d-allethrin treated mats. However, the registrant emphasized that this data was not submitted to support efficacy. The Agency will only review the product specific data (5.5% Metofluthrin).

Test substance
Thermacell Radius Zone Mosquito Repellent VI (5.5% metofluthrin liquid with wick and battery-powered heater) consisting of a Radius emitter with Metofluthrin cartridges. This product is an actively dispersed area repellent containing an active ingredient known to repel mosquitoes.

Test locations and dates
Efficacy was tested in two different mosquito rich habitats, one in Northern California and one in Eastern Louisiana, USA. Sites were chosen based on mosquito populations, vegetation types, and habitat evaluations performed by the Study Director. The sites differed in vegetative structure, water bodies and in both, species composition and relative abundance of host seeking mosquitoes present. A more detailed description of the sites and the dates of the studies are presented in Table 1.

Table 1. Study sites characteristics and dates of the studies

Site No.	**Date**	**State**	**Habitat**
1	20-23 May 2019	Louisiana	Freshwater and brackish marsh, swamp and hardwood forest
2	10-12 June, 2019	California	Riparian forest, freshwater marsh, irrigated fields

Environmental conditions, including ambient temperature, relative humidity and wind speed were measured at approximately 1-hour intervals throughout the duration of the study on all study days.

Test system information
Testing was conducted with field mosquitoes that were native to the test site locations.

Experimental design
In each of the two habitats (N. California and E. Louisiana), 12 distinct 20' x 20' plots with a minimum of 250' between any two plots and with relatively heterogeneous mosquito populations, were identified. In each habitat, treated and control plots were tested simultaneously across multiple plots. Each plot had 3 BioGents® Sentinel-2® mosquito traps, each placed at a 10' radius from the plot's center point (see Figure 1). This array created a test area of protection of 315 square feet (29.2 m^2). Each BG-Sentinel 2 trap was baited with Carbondioxide (BioGents pressure-reducing regulator at a flow rate of 0.5 kg/day/trap). In treated plots, the test material was placed at 10' radius from the plot's center point at 59 cm from the ground. All plots that were untreated controls didn't have test material on them. The cardinal orientations of each plot were determined by the Study Director with the intention of mitigating wind flow through the plot in order to limit the movement of emitted test material from the plot. Each plot was protected with wind barriers in the predominant direction of the wind, in order to reduce wind velocity in the plot. The Study Director determined that due to the presence of a uniform natural wind barrier of dense vegetation from which mosquitoes were likely to fly through in site 1, plots at site 1 were equipped with a single wind barrier 20' long x 10' tall directly adjacent to the natural wind barrier of dense vegetation. At site 2, the lack of homogeneity of plot location relative to natural wind barriers prompted the Study Director to implement the use of two-sided wind barriers, with each vertex of the barrier facing vectors of the oncoming airflow. These plots in site 2 were provided with wind screening consisting of natural vegetation and a 10' tall by 20' or 40' long temporary wall, to mimic a wind protected patio or the outdoor area adjacent to a building or protective vegetation.

Figure 1. Plot set up

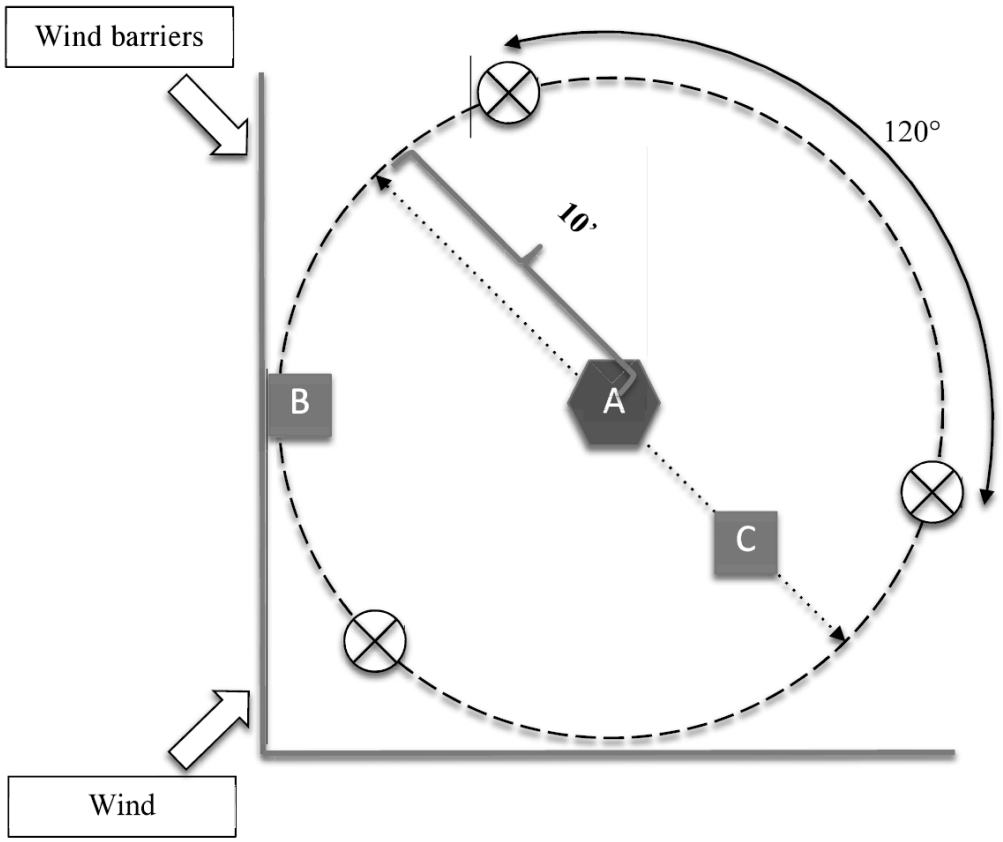

Figure 1. Test plot set-up and Area of Protection. **A** = Thermacell emitter at center of plot. **B** = limit of claimed Area of Protection (dashed circle). ⊗ = Trap locations evenly spaced around perimeter of Area of Protection. **C** = Diameter of Area of protection (20' dotted line) define the Area of Protection (315 square feet). Structure walls are optional temporary installations to control natural airflow, mimicking patios or other common outdoor recreational spaces flanked by structural or vegetative barriers on one or more sides.

Mosquito trapping, handling and identification

Mosquitoes were attracted to traps by carbon dioxide released at a similar rate of a human output via exhalation (approximately 0.5 kg/day). At the end of each exposure period, the trap capture bag was removed from each trap and immediately replaced with an empty capture bag to begin the next exposure period. Captured mosquitoes were then counted and identified to species and/or genus level. To expedite trap bag collection, mosquitoes in trap bags were emptied into plastic bags lined with a paper towel, sealed, and refrigerated in a cooler for later counting. All mosquito identifications were completed by the Study Director or Senior Entomologist, who consulted keys provided by local mosquito control agencies as needed. In some cases, specimens appearing to be from one of the more common species were identified to genus level only for expediency.

Test material handling and preparations for use

Test materials were stored in a locking closed cabinet at room temperature (21-25°C). Prior to each study, all Thermacell Radius Zone Repeller VI cartridges and emitters were inventoried and serial numbers were recorded. Each cartridge was then labeled with an identifying letter and weighed with protective plastics covering and the original plastic tape was retained. Test materials were "pre-vaporized", in accordance with communications with Thermacell representative, for 120 minutes (2 hours) prior to testing in an area distant from each site. Pre and post weights were recorded for this phase. Radius emitters were charged prior to each study day, given an identifying

number/letter, and serial numbers of each device were documented. At the beginning of each test date where test materials were used, each cartridge was inserted into its assigned emitter after removing the plastic tape and protective plastic coverings and brought to the assigned test site. The emitter was placed at the center of each plot, 59 cm from the ground. At the beginning of the determined pre-charge period of 15 minutes, each device was turned on and observed until visible vapor confirmed that test material began to be emitted from the device. Exposures began 15 minutes after the devices were activated. Devices were run during four periods of 1 hour, turned off immediately after each hourly collection of traps bags, and then turned back on. At the end of the 4 hours, all devices were turned off. Emitters were then collected, placed into individual plastic bags and weighed. Star/stop times, before and after pre-vaporization weights, and pre and post study weights were recorded.

Study set up

On day 1, all plots served as controls. Untreated control traps on day 1 served 3 functions:

1. To validate mosquito pressure was adequate to complete each test at each plot
2. To allow blocking of treatment and control assignments based on Day 1 plot capture rates in order to minimize bias in the probable ambient mosquito pressures at treated and control plots locations
3. To check for any mosquito pressure changes that might occur due to trapping or other factors between study days.

Day one: All 12 plots, from both sites, were controls

Day 2: Site 1 and Site 2 had 3 Metofluthrin plots and 6 control plots, each.

Day 3: Site 1 and Site 2, had 4 Metofluthrin plots and 6 control plots, each.

Within each site, two trap lines were established, consisting of one half (6 of the plots) for hourly sampling. A separate team was assigned to collect mosquitoes form each trap line. A single team would not have been capable of sampling 12 plots at hourly intervals. The two trap lines (traps 1-6 and traps 7-12) were geographically separated at each site.

Study Days 2 and 3. A total of 6 control and 6 treated plots were sampled in study Days with treatment. Day 3 treatment and control assignments were reciprocal of Day 2 assignments. Within each trap line, treatments were separated by a control. Each of the two trap lines per site consisted of 3 untreated control plots and 3 treated plots. I trap line included 2 Metofluthrin and 1-d Allethrin plot on Day 2, with the reciprocal arrangement on Day 3 (site1; at site 2, 4 of the six treated plots on each treated Day had Metofluthrin with the other being d-Allethrin). Treated plots were assigned to provide relatively equal exposure of each test material to Day 1 measured control mosquito pressure.

Distributions of test materials and controls among study plots on each study day within each of the two sites. In the table below, test materials indicated by their abbreviated name of their active ingredient. C= untreated control, A=d-Allethrin (MR300 Mosquito Repeller) and M=Metofluthrin (Radius Zone Repeller). Shaded cells show plots with data excluded form at least one exposure period on the indicated study Day

Table 2. Treatment distributions among plots

	Plot											
	1	2	3	4	5	6	7	8	9	10	11	12
SITE 1												
Day 1	C	C	C	C	C	C	C	C	C	C	C	C
Day 2	M	C	A	C	M	C	A	C	M	C	A	C
Day 3	C	A	C	M	C	A	C	M	C	A	C	M
SITE 2												
Day 1	C	C	C	C	C	C	C	C	C	C	C	C
Day 2	M	C	M	C	A	C	C	M	A	C	C	M
Day 3	C	A	C	M	C	M	A	C	C	M	M	C

Data excluded due to technical issues, Site 2:
Day 1:

- Exposure 1,2
  - Plot 1 (CO_2 release low)
  - Plot 2 (CO_2 release rate)

Day 3:

- Exposure 1
  - Plot 2 (CO_2 release abbreviated)
  - Plot 7 (CO_2 release abbreviated)
  - All plots (Control trap counts low)
- Exposure 2-4
  - Plot 4 (emitter under-charged)
  - Plot 6 (emitter under-charged)
  - Plot 10 (emitter under-charged)

Data summary and analyses
The performances of the test materials were assessed with reference to a common set of untreated plots, but each was analyzed separately from the other. Moreover, comparing the efficacy of the two test materials was not an objective of the study.
The data includes 288 observations (182 for controls and 56 for Metofluthrin) of the numbers of mosquitoes captured at each of the 12 plots, for four one-hour exposures, throughout three days of testing, at two different sites. There were five categorical variables measured: site, test day, exposure, plot, treatment, exposure duration, and number of mosquitoes captured per plot. Due to several plots experiencing trap or emitter errors at site 2, 24 (9 for Metofluthrin) observations were excluded from the analysis; the final full data set includes 264 observations (47 observations for Metofluthrin).
The data was analyzed using the statistical software R and the associated application RStudio to logistic regression. The standard approach to model biological count data involves the use of a Poisson or negative distribution. However, for a Poisson distribution to be the best choice for a model, the variance of the data needs to be exactly equal to the mean, which means there is zero overdispersion. In count data form experiments vulnerable to overdispersion, the use of a Poisson distribution can lead to anti-conservative measures of standard error. To produce a properly fitted model for overdispersed count data, a negative binomial distribution is a better choice. The registrant state that because their data exhibited strong overdispersion they used a negative binomial distribution for their models.

Three models were created:

1. Individual regressions on exposure-specific data for both sites, which provided estimates for repellent performance by exposure for each of the two treatments, at each of the two sites. This generated a picture of the temporal consistency of repellent performance. In this model, the dependent variable was number of mosquitoes, the explanatory variables were plot and treatment, and exposure duration was used as an offset factor. The model was represented by the following equation:

$$\ln(\lambda) = \mu + \alpha_P + \delta_{treat} + \ln(\text{min}) + \varepsilon,$$

where λis the estimated number of mosquitoes,
α_P is the categorical effect of plot,
δ_{treat} is the categorical effect of exposure,
is the treatment effect (the measure of proportional repellency in log scale),
min is the exposure duration,
and ε is an error term to account for overdispersion

2. Individual regressions on site-specific data for both sites. This provides a contrast in repellent performance across the two sites. In this model, the dependent variable was Number of Mosquitoes, the explanatory variables were plot, exposure, and treatment, and exposure duration was used as an offset factor. The model took the following form:

$$\ln(\lambda) = \mu + \alpha_P + \beta_E + \delta_{treat} + \ln(min) + \varepsilon,$$

where λ is the estimated number of mosquitoes,
α_P is the categorical effect of plot,
β_E is the categorical effect of exposure,
δ_{treat} is the treatment effect (the measure of proportional repellency in log scale),
min is the exposure duration,
and ε is an error term to account for overdispersion.

3. One regression that combined 264-observation data set. This provides an estimate for the overall mean efficacy of each of the two repellents. In this model, the dependent variable number of mosquitoes and the explanatory variables were plot, exposure, site and treatment, and exposure duration was used as an offset factor. The model took the following form:

$$\ln(\lambda) = \mu + \alpha_P + \beta_E + \gamma_S + \delta_{Treat} + \ln(min) + \varepsilon,$$

where λ is the estimated number of mosquitoes,
α_P is the categorical effect of plot,
β_E is the categorical effect of exposure,
γ_S is the categorical effect of site,
δ_{Treat} is the treatment effect (the measure of proportional repellency in log scale),
min is the exposure duration
and ε is an error term to account for overdispersion.

In all of these models, Test Day was not used as an explanatory variable due asymmetric exclusion of data, which caused excessive inflation of variance.

Calculation of percent repellency
The following formula was used to determine the percent repellency for a particular treatment:

$$\text{Percent repellency} = (1\text{-e }\hat{}(T))*100$$

Where "e" is the Euler's number
And T is the regression coefficient for that treatment

The regression coefficients are on log scale; therefore, to obtain values for percent repellency on a linear scale, the regression coefficients were exponentiated.

Deviations to the protocol
There were 6 deviations to the protocol:

- The researcher did not have the Certificate of analysis (C of A) on file for the test material that were from certain lot, at the beginning of the study. The sponsor subsequently provided the C of A prior to the completion of the final study report. Multiple shipments of the test substance were provided, and it was not originally noted that they were from different production lots. The Study Director (SD) concludes that the same formulation laboratory and personnel produced both, the characterized and uncharacterized lots within the same general time frame, and judged reasonable to proceed with testing material from both lots in advance of receiving the second C of A. The SD determined that the quality of the data set was not adversely affected. The reviewer agrees with this reasoning. However, proper documentation of the test substance should be ensured before starting trials.
- Metofluthrin emitters were not given a unique code, as stated in the protocol, however, they have unique serial numbers. Those serial numbers were not recorded on the Chain of Custody paperwork received from the sponsor. Devices were not assigned a number but were marked as used with number plot where they were used and date of use, so they weren't accidentally used again. Use of unique identifiers were provided permitted simpler, more direct accounting and tracking of test materials. A new labeling system was implemented. The SD concluded that the quality of the data set was not affected. The reviewer agrees to this reasoning. However, proper labeling of test materials before, during and after trials should be ensured during the preparation phase of the trials or create labels that allow flexibility to be filled right before the

trial.

- Stability tests were pending completion at the time of use of the study materials in the study. The SD determined to proceed with the beginning of the study without results of the stability tests. The active ingredient is well known for stability and given their recent production dates relative to the study onset, the study director judged them suitable for testing. The SD concluded that the quality of the data set is not adversely affected. The reviewer agrees with this reasoning. However, it is recommended that stability testing be completed before the study and this information be included in the final report, if the data is available.
- A single wind-screening structure wall was employed at site 1, rather than the given options of 0 or 2 because the natural forest screened one of the directions of wind flow, and a single wall was installed perpendicular to the forest edge. The registrant assumes that this adjustment avoided excessive screening of the study plots, likely facilitating access to the plots by foraging mosquitoes, and had no impact in the quality of the data set. The reviewer agrees with this reasoning. However, the Agency recommends that future studies should have consistent methodology at all sites.
- Treatment not specified on trap bag labels in advance. The registrant states that specifying treatment on bag labels prevented them from creating finalized labels in advance of assigning treatments to plots on arrival at the sites, which was problematic. This changed was approved by the study director on order to improve data quality, by allowing pre-made tags to be used, which reduced the likelihood of errors and in identifying samples, while also allowing flexibility in assigning treatment to plots on the basis of real world conditions. In addition, treatment labeling of trap bag collections was redundant to contemporaneous records of treatment assignments by plot. Moreover, while treatment labeling of trap bags was originally included from an abundant of caution regarding treatment records, omitting treatment information from trap bag labels also improved blinding during trap counts. The SD concluded the quality of the dataset is not adversely affected. The reviewer agrees with this reasoning, and the trap bags labels were correctly identified in the end, however this is another labeling error that should have been addressed during the study preparation phase.
- At site 2, technical issues reduced the collection of mosquitoes and the dissemination of materials on days 1 and 3. On Day 1, there were lower than intended CO_2 emission rates at Plot 1 in Period 1 and Plot 2 in Periods 1 and 2. Similarly, on Day 3, Period 1, CO_2 releases began 5 min late at Plot 2 and 20 min late at Plot 7. In addition, in period 4, it was observed during some exposures that the indicator lights on some Radius emitters were off, indicating loss power. On Day 1, there were improper regulator settings. On Day 3, low CO_2 levels; low battery charge in radius devices. CO_2 regulator settings were corrected and filled tanks were substituted in upon detection of the issues. Similarly, unpowered emitters were immediately replaced with charged units, and the replacements times were recorded. The SD concluded that data was affected in three ways:
    - On Day 1, trap count data from 3 of the 48 control exposure periods were excluded based on inadequate CO_2 levels.
    - On day 3, two exposure periods were truncated due to delay in CO_2 provisioning, but the registrant states that those deviations are unlikely to influence data quality and were readily accommodated statistically by their analytical model.
    - On day 3, because the times of onset of the Radius device power failures were not precisely known, data from all potentially affected exposure periods (N=23) were excluded for analyses. While these outcomes reduced the number of traps counts in the data set, the remaining data set was sufficient for statistical analysis and product evaluation. The SD concludes that this positive outcome despite the technical issues described here was abetted by the relative low variability in consistently Radius Zone Repeller VI efficacy across exposure periods.

  The reviewer disagrees about the impact of technical issues, including the incorrect flow of CO_2 and uncharged devices. The above-mentioned issues are important and constitute deficiencies on the execution of the study. Excluding data from all plots and all sites affects sample size and replication, as 9 out 16 observations for Metofluthrin on Day 3, at Site 2, were excluded.

(3) **Results**:

Field Environmental conditions

Environmental conditions at both study sites were as shown in table XX:

Table 2. Environmental conditions at the two study sites

Variable	Site 1: Louisiana			Site 2: California		
	Mean	Median	Range	Mean	Median	Range
Temperature (°C)	24.22	24	21-32	24.66	25	17-38
Relative humidity (%)	88.5	91	56-94	75.96	76	46-91
Wind speed (kph)	0.15	0	0-2.6	0	0	0

Weight of test materials before and after the study
The test materials were weighed before and after use in the study. The seven Radius Zone VI products emanated between 0.0 and 1.1. grams across the approximate 4- hour exposure period. Test materials were not weighed at the end of every hour exposure period.

The below Table summarizes weights of the metofluthrin devices before and after the 2-hour pre-vaporization or pre-burn period for site 1 (May) and Site 2 (June).

Table 3. Weight of expended active ingredient during pre-vaporization

Test material ID	Pre-vaporization date	Pre-vaporization start time	Pre-vaporization stop time	Initial weight	Post pre-vaporization weight	Weight lost
5.5m 1	21-May-19	17:12	19:12	30.6	29.9	0.7
5.5m 2	21-May-19	17:12	19:12	30.5	29.8	0.7
5.5m 3	21-May-19	17:12	19:12	30.6	29.8	0.8
5.5m 4	23-May-19	17:09	19:09	30.6	29.8	0.8
5.5m 5	23-May-19	17:09	19:09	30.6	29.8	0.8
5.5m 6	23-May-19	17:09	19:09	30.5	29.7	0.8
5.5m 7	11-Jun-19	14:10	16:10	30.6	29.8	0.8
5.5m 8	11-Jun-19	14:10	16:10	30.5	29.6	0.9
5.5m 9	11-Jun-19	14:10	16:10	30.7	29.9	0.8
5.5m 10	11-Jun-19	14:10	16:10	30.6	29.9	0.7
5.5m 11	12-Jun-19	17:15	18:50	30.5	30.3	0.2
5.5m 12	12-Jun-19	17:15	18:50	30.5	30.1	0.4
5.5m 13	12-Jun-19	17:15	19:00	30.5	30.3	0.2
5.5m 14	12-Jun-19	17:15	19:00	30.4	30.1	0.3

Number and species of mosquitoes collected
Mosquitoes were abundant and diverse in both study sites. Site 1 had more than 14,000 mosquitoes of at least 16 species were trapped across the three study days. *Culex* were the most diverse (5 species) and abundant (>73% of specimens collected). *Anopheles crucians* was the second most abundant species, followed by *Coquillettidia perturbans.* Site 2 had significantly less species than site 1, and only One species in common (*Aedes vexans*).

Table 4. Species abundance and composition at study sites

Mosquito species	**Site 1**		**Site 2**	
	control	**test**	**control**	**test**
*Aedes genus*1	35	4		

Aedes melanimon			11118	991
Aedes nigromaculatus			1283	176
Aedes sollicitans	153	10		
Aedes vexans	2	0		
Anopheles crucians	1212	73		
Anopheles freeborni			301	98
Anopheles punctipennis			107	0
Anopheles quadrimaculatus	7	0		
Coquillettidia perturbans	1446	64		
Culex genus[2]	11307	415		
Culex erraticus	83	0		
Culex erythrothorax			3	0
Culex quinquefasciatus	39	0		
Culex restuans	3	0		
Culex salinarius	11	0		
Culex tarsalis	1	0	144	47
Culiseta inornata			1	1
Mansonia dyari	2	0		
Orthopodomyia signifera	1	0		
Psorophora ciliata	1	0		
Psorophora columbiae	13	2		
Psorophora howardi	9	0		
Totals	14325	568	19452	1665

[1] Principal species: *Aedes sollicitans*
[2] Principal species: *Cx. erraticus, Cx. quinquefasciatus* and *Cx. salinarius*

Capture rates
Mosquito capture rates were for the most part >1 mosquito/minute, except for some plots at Day 3 at both study sites. See table 5.

Table 5. Mosquito pressure

	Exposure period			
	1	2	3	4
SITE 1				
Mosquito pressure by Exposure				
Mean of control plots Day 1	3.15 ± 1.42	2.95 ± 1.82	2.75 ± 1.20	2.79 ± 1.51
Mean of control plots Day 2	5.61 ± 2.71	2.80 ± 1.95	1.98 ± 1.06	2.35 ± 1.26
Mean of control plots Day 3	1.98 ± 1.50	0.93 ± 0.45	0.52 ± 0.40	0.18 ± 0.17
Mosquito pressure by Day				
Mean of control plots Day 1	2.91 ± 0.18			
Mean of control plots Day 2	3.19 ± 1.65			
Mean of control plots Day 3	0.90 ± 0.78			
SITE 2				
Mosquito pressure by Exposure				
Mean of control plots Day 1	1.29 ± 0.74	6.79 ± 3.79	5.57 ± 3.01	3.00 ± 1.80
Mean of control plots Day 2	0.71 ± 0.76	4.96 ± 3.90	5.78 ± 4.12	3.00 ± 1.71
Mean of control plots Day 3	0.26 ± 0.08[1]	2.71 ± 1.68	3.38 ± 1.88	2.32 ± 1.23
Mosquito pressure by Day				
Mean of control plots Day 1	4.16 ± 2.48			
Mean of control plots Day 2	3.61 ± 2.26			
Mean of control plots Day 3	2.17 ± 1.35			

[1] Data from this exposure period were exluded on the basis of the combination of two concerns: comparatively low ambient mosquito pressue associated with problem with CO2 regulators that resticted CO2 release in Plot 3 (Control) and Plot 7 (d-allethrin).

Repellent efficacy

Combined model

The registrant used logistic regression of trap capture counts to analyze the magnitude of the treatment effect along with the effects of the other discrete variables determined by their study design (plot, exposure period, test date and site). Table 6 presents analysis if deviance metrics for each effect. Higher deviance values indicate that less variance is explained by a model that includes only the tabulated factor. The maximum single probability values for any effect was $P<2.2$ e-16.

Table 6. Analysis of Deviance for combined regression on trap capture counts

	Df	Deviance	Resid. Df	Resid. Dev	Pr(>Chi)
NULL			257	45572	
Site	1	1645	256	43927	< 2.2e-16
Exposure Period	6	5923.1	250	38004	< 2.2e-16
Plot	22	8982.7	228	29022	< 2.2e-16
Treatment	2	12091.6	226	16930	< 2.2e-16

Repellency by site and exposure period

Key repellency findings for the product for the entire study and each site are characterized as follows (Mean ± SE):

- Study repellency averaged 83.17±0.02%
- Site 1 repellency averaged 85.91±0.02%
- Site 2 repellency averaged 78.55 ±0.02%
- Average repellency was above 75% in six of the eight exposure periods across the two sites (range 69-93%)

Table 7. Repellency by site and exposure period

Site	Exposure period			
	1	2	3	4
Site 1	78.24±0.04	88.32±0.04	89.11±0.05	87.05±0.06
Site 2	92.83±0.07	73.81±0.03	69.33±0.03	80.43±0.02

(4) **Conclusion**: After 2 hours of pre-vaporization and 15 minutes of activation, there was greater than or equal to 75% repellency. This MRID is **acceptable** to support efficacy claims of increasing the area of coverage from 10' to 20' for Thermacell Mosquito Zone Repeller VI for protection against mosquitoes. However, there are some issues with this study that should be addressed for future studies:

- Exclusion of data. In general, data should not be excluded. Exclusions should be discussed with the Agency before the submission of the study.
- Exposure time. The registrant did 4 sequential exposures of 1 hour each in the same plot on the same day. The Agency recommends that treatment tests should only occur once daily (single exposure/plot/day). Plots should only be reused twice, and a complete rotation of treatments/controls is recommended. The second run of the plot should not occur on the same day of the first run. Exposure times and all pre-burning times need to correspond to the label DFU.
- This study tested 2 different test substances with two different active ingredients at both study sites: Thermacell Mosquito Zone Repeller VI (5.5% metofluthrin) and Thermacell M300 (21.9% d-Alletrin). Future final study reports should include the steps taken to avoid cross contamination during handling/testing of the test substance.
- The registrant used one wall structure and a natural barrier of trees as the other side of the wall for all plots in Study site 1 and used a two-wall structure at site 2. The Agency recommends that future study methodology be consistent across sites.
- The registrant used a CO_2 rate of 0.5 Kg/Day to simulate the CO_2 output of a human. For future studies, the Agency recommends using a CO_2 rate of 500ml/min, which represents the high output of a human.

IV. EXECUTIVE DATA SUMMARY:

After 2 hours of pre-vaporization and 15 minutes of activation, there was greater than or equal to 75% repellency. The data submitted is acceptable to increase the area of coverage from 10' to 20' for Thermacell Mosquito Zone Repeller VI. The study had several issues that should be addressed for future studies. Specific recommendations for future studies are described in greater detail at the conclusion section of this MRID.

V. LABEL RECOMMENDATIONS:

(1) List changes to the directions for use: A 2-hour initial burn off time should be added to the label.

(2) The following marketing claims are acceptable: N/A

(3) The following marketing claims are unacceptable: N/A

(4) The following MRIDs should be removed from the data matrix, as they are classified as "unacceptable" to support the product: N/A

(5) Note to PM: The following diseases were already listed in marketing claims on the previously approved label for the 10 foot coverage: Chikungunya, dengue, Zika and La Crosse encephalitis. In the currently submitted test to support the 20 foot coverage, while species from the same genera of the vectors of these diseases were present, the specific species vectors of Chikungunya, Dengue, Zika (*Aedes albopictus, Aedes aegypti*) and La Crosse encephalitis (*Aedes triseriatus, Aedes albopictus* and *Aedes japonicus*) were not.